ENDOCRINE ASSESSMENT OF IMPOTENCE - PITFALLS OF MEASURING SERUM TESTOSTERONE WITHOUT SEX-HORMONE-BINDING GLOBULIN

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Endocrine assessment of impotence – pitfalls of measuring serum testosterone without sex-hormone-binding globulin

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Summary: The pitfalls of measuring only total serum testosterone are illustrated by a 52 year old man whose hyperprolactinaemia was associated with normal total serum testosterone but a raised sex-hormone-binding globulin, giving a low free testosterone. Prolactin suppression with bromocriptine normalized sex-hormone-binding globulin and free testosterone, and restored potency and energy after 30 years of impotence and tiredness.

Introduction

Impotence is a common and distressing symptom that may present to general practitioners or to a variety of different specialists.[1-3] To highlight the need for full endocrinological assessment of patients with impotence, we report a 52 year old man with a 30 year history of impotence whose total serum testosterone was misleadingly normal, but whose free testosterone was low by virtue of his raised sex-hormone-binding globulin (SHBG) levels. Treatment of his microprolactinoma normalized SHBG and free testosterone, and restored potency. Endocrinological assessment of impotence should include calculation of free testosterone by measurement of SHBG.

Case report

A 52 year old man was referred to a urologist by his general practitioner with a 4-year history of erectile failure. Direct questioning revealed that he had been impotent for 30 years, achieving only partial erections after protracted foreplay. He was able to ejaculate normally (he had fathered three children). He and his wife had volunteered the problem once before, 4 years earlier, when they had received psychosexual counselling (without investigation) to no avail. Over the years he had been investigated for a variety of vague somatic symptoms dominated by profound tiredness and weakness. On assessment, he was being treated with clomipramine 25 mg thrice daily for tiredness presumed to be secondary to depression. Urological examination was unremarkable but he was found to have an elevated serum prolactin of 2343 mU/l. Clomipramine was stopped but his symptoms were not improved so he was referred to an endocrinologist.

On endocrinological assessment, 6 months after stopping clomipramine, the patient's impotence was unchanged. He considered his libido to be normal, and denied headache, breast enlargement or tenderness, galactorrhoea, reduced beard growth, skin change, or postural dizziness. On examination he was noted to have very fine facial skin. There were no features of Cushing's disease or acromegaly, there was no gynaecomastia or galactorrhoea, and no postural hypotension. His penis was normal, and both testes were firm and of normal volume. He was not obviously depressed. Total thyroxine and thyrotrophin were normal at 94 (reference range 60–145) nmol/l and 2.0 (reference range 0.1–5.5) mU/l, respectively. Cortisol rose after 250 μg tetracosactrin from 486 to 821 (normal > 550) nmol/l, and gonadotrophins and oestradiol were within the quoted normal range, follicle stimulating hormone 6.7 U/l, luteinizing hormone (LH) 3.2 (reference range for both 1.5–9.0) U/l, oestradiol 97 (reference range < 200) pmol/l. Serum prolactin was markedly elevated at 2,390 (reference range 60–390) mU/l, and although total testosterone was normal at 11.2 (reference range 10–30) nmol/l, SHBG was high at 57 (reference range 6–45) nmol/l, giving a low free testosterone of 19.5 (reference range > 22) nmol/l. Visual fields were full but pituitary magnetic resonance imaging suggested a microadenoma. He was treated with the dopamine agonist bromocriptine 2.5 mg thrice daily, which within 6 weeks normalized prolactin to 88 mU/l. Total testosterone increased to 23.0 nmol/l and SHBG fell, giving a normal free testosterone of 34 nmol/l. At this time the patient's chronic tiredness had

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resolved, his libido was increased, and for the first time in 30 years, he was able to sustain normal erections.

Discussion

Impotence may be defined as inability to attain an erection of sufficient rigidity for vaginal penetration in 50% or more of attempts.[4] Erectile insufficiency after a period of normal sexual functioning is referred to as secondary impotence. Despite his 30-year history of impotence, our patient was rapidly improved after identification and treatment of his hyperprolactinaemia. This illustrates several important points about the management of impotence. Impotence, even of many years' duration, may not be volunteered by patients and cannot be excluded by the patient's ability to father children. Impotence should never be dismissed as being of psychological origin without full examination and adequate endocrine assessment. General assessment should include a search for diabetes, vascular disease, neuropathy, uraemia, occult malignancy (especially prostate carcinoma), haemochromatosis and drug and alcohol history. Assessment should also be made for androgen deficiency: loss of libido, loss of muscle bulk, and loss of secondary sexual hair, together with voice change, fine skin and reduced testicular volume. A search should be made for causes of primary and secondary gonadotrophin deficiency, such as Kallman's syndrome, acromegaly and Cushing's disease. As well as random blood glucose, electrolytes, liver function tests, and investigations prompted by physical signs, thyroid function, gonadotrophins, prolactin and serum testosterone should always be measured.

This patient illustrates well the occasional pitfall of relying on total serum testosterone (which was within the reference range) when androgen deficiency is suspected. Sex-hormone-binding globulin is androgen-regulated and therefore often raised when testosterone is low.[5] As in this case, total serum testosterone may be normal while free testosterone is unequivocally low. Measurement of SHBG with calculation of free testosterone will avoid this problem. Hyperprolactinaemia causes suppression of the hypothalamic–pituitary–gonadal axis perhaps by opioid-mediated inhibition of normal pulsatile secretion of LH,[6] the stimulus to testosterone secretion by Leydig cells. Gonadotrophin levels within the reference range in the presence of low free testosterone, in this patient, were inappropriate and suggest a hypothalamic or pituitary cause for his androgen deficiency. Bromocriptine, by virtue of its dopamine agonist properties, inhibits prolactin secretion by lactrotrophs and usually restores prolactin levels to normal.[7] Not only was our patient's impotence cured by treatment of his hyperprolactinaemia, but his long-standing weakness and tiredness (presumably secondary to chronic androgen deficiency) also responded to normalization of testosterone with bromocriptine.

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